#5

SEQUENCE LISTING

<110> Bristol-Myers Squibb
       Bristol-Myers Squibb

<120> MODULATORS OF BRUTON'S TYROSINE KINASE AND BRUTON'S TYROSINE KINASE
INTERMEDIATES AND METHODS FOR THEIR IDENTIFICATION AND USE IN THE TREATMENT AND
PREVENTION OF OSTEOPOROSIS AND RELATED DISEASE STATES

<130> D0032 NP

<140> 10/045,202
<141> 2001-10-22

<150> 60/242,471
<151> 2000-10-23

<160> 12

<170> PatentIn version 3.1

<210> 1
<211> 2560
<212> DNA
<213> Human

<400> 1

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gatgttgaga agatcacttg tgttgaaaca gtggttcctg aaaaaaatcc tcctccagaa     360

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aggttccctt atcccttcca ggttgtatat gatgaagggc ctctctacgt cttctcccca     480

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gtgtctgtgt ttgctaaatc cacaggggac cctcaagggg tgatacgtca ttatgttgtg   1140

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<210> 2
<211> 659
<212> PRT
<213> Human

<400> 2

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            20   25   30

Thr Val His Lys Leu Ser Tyr Tyr Glu Tyr Asp Phe Glu Arg Gly Arg
            35   40   45

Arg Gly Ser Lys Lys Gly Ser Ile Asp Val Glu Lys Ile Thr Cys Val
        50   55   60

Glu Thr Val Val Pro Glu Lys Asn Pro Pro Glu Arg Gln Ile Pro
65   70   75   80

Arg Arg Gly Glu Glu Ser Ser Glu Met Glu Gln Ile Ser Ile Ile Glu
                85   90   95

Arg Phe Pro Tyr Pro Phe Gln Val Val Tyr Asp Glu Gly Pro Leu Tyr
            100   105   110

Val Phe Ser Pro Thr Glu Glu Leu Arg Lys Arg Trp Ile His Gln Leu
        115   120   125

Lys Asn Val Ile Arg Tyr Asn Ser Asp Leu Val Gln Lys Tyr His Pro
    130   135   140

Cys Phe Trp Ile Asp Gly Gln Tyr Leu Cys Cys Ser Gln Thr Ala Lys
145   150   155   160

Asn Ala Met Gly Cys Gln Ile Leu Glu Asn Arg Asn Gly Ser Leu Lys
            165   170   175

Pro Gly Ser Ser His Arg Lys Thr Lys Lys Pro Leu Pro Pro Thr Pro
            180   185   190

Glu Glu Asp Gln Ile Leu Lys Lys Pro Leu Pro Pro Glu Pro Ala Ala
    195   200   205

3

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Ala Pro Val Ser Thr Ser Glu Leu Lys Lys Val Val Ala Leu Tyr Asp
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Tyr Phe Ile Leu Glu Glu Ser Asn Leu Pro Trp Trp Arg Ala Arg Asp
                245             250             255

Lys Asn Gly Gln Glu Gly Tyr Ile Pro Ser Asn Tyr Val Thr Glu Ala
            260             265             270

Glu Asp Ser Ile Glu Met Tyr Glu Trp Tyr Ser Lys His Met Thr Arg
            275             280             285

Ser Gln Ala Glu Gln Leu Leu Lys Gln Glu Gly Lys Glu Gly Gly Phe
    290             295             300

Ile Val Arg Asp Ser Ser Lys Ala Gly Lys Tyr Thr Val Ser Val Phe
305             310             315             320

Ala Lys Ser Thr Gly Asp Pro Gln Gly Val Ile Arg His Tyr Val Val
            325             330             335

Cys Ser Thr Pro Gln Ser Gln Tyr Tyr Leu Ala Glu Lys His Leu Phe
            340             345             350

Ser Thr Ile Pro Glu Leu Ile Asn Tyr His Gln His Asn Ser Ala Gly
    355             360             365

Leu Ile Ser Arg Leu Lys Tyr Pro Val Ser Gln Gln Asn Lys Asn Ala
    370             375             380

Pro Ser Thr Ala Gly Leu Gly Tyr Gly Ser Trp Glu Ile Asp Pro Lys
385             390             395             400

Asp Leu Thr Phe Leu Lys Glu Leu Gly Thr Gly Gln Phe Gly Val Val
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Lys Tyr Gly Lys Trp Arg Gly Gln Tyr Asp Val Ala Ile Lys Met Ile
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4

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Lys Glu Gly Ser Met Ser Glu Asp Glu Phe Ile Glu Glu Ala Lys Val
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Thr Lys Gln Arg Pro Ile Phe Ile Ile Thr Glu Tyr Met Ala Asn Gly
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Cys Leu Leu Asn Tyr Leu Arg Glu Met Arg His Arg Phe Gln Thr Gln
            485             490             495

Gln Leu Leu Glu Met Cys Lys Asp Val Cys Glu Ala Met Glu Tyr Leu
        500             505             510

Glu Ser Lys Gln Phe Leu His Arg Asp Leu Ala Ala Arg Asn Cys Leu
        515             520             525

Val Asn Asp Gln Gly Val Val Lys Val Ser Asp Phe Gly Leu Ser Arg
    530             535             540

Tyr Val Leu Asp Asp Glu Tyr Thr Ser Ser Val Gly Ser Lys Phe Pro
545             550             555             560

Val Arg Trp Ser Pro Pro Glu Val Leu Met Tyr Ser Lys Phe Ser Ser
            565             570             575

Lys Ser Asp Ile Trp Ala Phe Gly Val Leu Met Trp Glu Ile Tyr Ser
            580             585             590

Leu Gly Lys Met Pro Tyr Glu Arg Phe Thr Asn Ser Glu Thr Ala Glu
        595             600             605

His Ile Ala Gln Gly Leu Arg Leu Tyr Arg Pro His Leu Ala Ser Glu
    610             615             620

Lys Val Tyr Thr Ile Met Tyr Ser Cys Trp His Glu Lys Ala Asp Glu
  625             630             635             640

Arg Pro Thr Phe Lys Ile Leu Leu Ser Asn Ile Leu Asp Val Met Asp
            645             650             655
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5

Glu Glu Ser

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<211> 2468
<212> DNA
<213> Murine

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gatgttgaga agatcacctg tgttgaaaca gtaattcctg aaaaaaatcc cccaccagaa   360

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gtgtctaaac aaaacaaaaa cgcgccttct actgcaggcc tgggctatgg atcatgggaa   1320

attgatccaa aggacctcac cttcttgaag gagcttggga ctggacaatt cggtgtcgtg   1380

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.6

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atggctaatg gctgcctctt gaactacctg agggagatgc ggcaccgctt ccagacacag    1620

cagctgcttg agatgtgcaa agatgtctgt gaagcaatgg aatacttgga gtcgaagcag    1680

ttccttcaca gagacctggc agctcgaaac tgtttggtaa cgatcaagg agttgtgaaa    1740

gtatctgact ttggcctgtc taggtatgtc cttgatgatg agtacaccag ctctgtaggc    1800

tccaagtttc cagtccggtg gtctccacca gaagtgctta tgtatagcaa gttcagcagc    1860

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ccgtatgaga gatttactaa cagtgagaca gcagaacaca ttgctcaagg cttacgtctc    1980

tacaggcctc atctggcatc agagagggta tataccatca tgtacagctg ctggcacgag    2040

aaagcagatg aacgtcctag tttcaaaatt ctcttgagta acattctaga tgtgatggat    2100

gaagaatcct gagctggctg ctaagctccg tggatctcct cctctctcct acaaaaccta    2160

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<210>   4
<211>   659
<212>   PRT
<213>   Murine

<400>   4

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Met Ala Ala Val Ile Leu Glu Ser Ile Phe Leu Lys Arg Ser Gln Gln
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Lys Lys Lys Thr Ser Pro Leu Asn Phe Lys Lys Arg Leu Phe Leu Leu
            20                  25                  30


Thr Val His Lys Leu Ser Tyr Tyr Glu Tyr Asp Phe Glu Arg Gly Arg
            35                  40                  45
```

7

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Arg Gly Ser Lys Lys Gly Ser Ile Asp Val Glu Lys Ile Thr Cys Val
 50                55              60

Glu Thr Val Ile Pro Glu Lys Asn Pro Pro Glu Arg Gln Ile Pro
 65                70              75              80

Arg Arg Gly Glu Glu Ser Ser Glu Met Glu Gln Ile Ser Ile Ile Glu
                85              90              95

Arg Phe Pro Tyr Pro Phe Gln Val Val Tyr Asp Glu Gly Pro Leu Tyr
                100             105             110

Val Phe Ser Pro Thr Glu Glu Leu Arg Lys Arg Trp Ile His Gln Leu
                115             120             125

Lys Asn Val Ile Arg Tyr Asn Ser Asp Leu Val Gln Lys Tyr His Pro
     130             135             140

Cys Phe Trp Ile Asp Gly Gln Tyr Leu Cys Cys Ser Gln Thr Ala Lys
145             150             155             160

Asn Ala Met Gly Cys Gln Ile Leu Glu Asn Arg Asn Gly Ser Leu Lys
                165             170             175

Pro Gly Ser Ser His Arg Lys Thr Lys Lys Pro Leu Pro Pro Thr Pro
                180             185             190

Glu Glu Asp Gln Ile Leu Lys Lys Pro Leu Pro Pro Glu Pro Thr Ala
                195             200             205

Ala Pro Ile Ser Thr Thr Glu Leu Lys Lys Val Val Ala Leu Tyr Asp
     210             215             220

Tyr Met Pro Met Asn Ala Asn Asp Leu Gln Leu Arg Lys Gly Glu Glu
225             230             235             240

Tyr Phe Ile Leu Glu Glu Ser Asn Leu Pro Trp Trp Arg Ala Arg Asp
                245             250             255

Lys Asn Gly Gln Glu Gly Tyr Ile Pro Ser Asn Tyr Ile Thr Glu Ala
                260             265             270

Glu Asp Ser Ile Glu Met Tyr Glu Trp Tyr Ser Lys His Met Thr Arg
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8

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Ser Gln Ala Glu Gln Leu Leu Lys Gln Glu Gly Lys Glu Gly Gly Phe
    290                 295                 300

Ile Val Arg Asp Ser Ser Lys Ala Gly Lys Tyr Thr Val Ser Val Phe
305                 310                 315                 320

Ala Lys Ser Thr Gly Glu Pro Gln Gly Val Ile Arg His Tyr Val Val
                325                 330                 335

Cys Ser Thr Pro Gln Ser Gln Tyr Tyr Leu Ala Glu Lys His Leu Phe
                340             345                 350

Ser Thr Ile Pro Glu Leu Ile Asn Tyr His Gln His Asn Ser Ala Gly
            355             360                 365

Leu Ile Ser Arg Leu Lys Tyr Pro Val Ser Lys Gln Asn Lys Asn Ala
    370                 375             380

Pro Ser Thr Ala Gly Leu Gly Tyr Gly Ser Trp Glu Ile Asp Pro Lys
385                 390                 395                 400

Asp Leu Thr Phe Leu Lys Glu Leu Gly Thr Gly Gln Phe Gly Val Val
            405                 410                 415

Lys Tyr Gly Lys Trp Arg Gly Gln Tyr Asp Val Ala Ile Lys Met Ile
            420                 425                 430

Arg Glu Gly Ser Met Ser Glu Asp Glu Phe Ile Glu Glu Ala Lys Val
            435                 440                 445

Met Met Asn Leu Ser His Glu Lys Leu Val Gln Leu Tyr Gly Val Cys
    450                 455                 460

Thr Lys Gln Arg Pro Ile Phe Ile Ile Thr Glu Tyr Met Ala Asn Gly
465                 470                 475                 480

Cys Leu Leu Asn Tyr Leu Arg Glu Met Arg His Arg Phe Gln Thr Gln
                485                 490                 495

Gln Leu Leu Glu Met Cys Lys Asp Val Cys Glu Ala Met Glu Tyr Leu
            500                 505                 510
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9

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Glu Ser Lys Gln Phe Leu His Arg Asp Leu Ala Ala Arg Asn Cys Leu
    515             520             525


Val Asn Asp Gln Gly Val Val Lys Val Ser Asp Phe Gly Leu Ser Arg
    530             535             540


Tyr Val Leu Asp Asp Glu Tyr Thr Ser Ser Val Gly Ser Lys Phe Pro
545             550             555             560


Val Arg Trp Ser Pro Pro Glu Val Leu Met Tyr Ser Lys Phe Ser Ser
            565             570             575


Lys Ser Asp Ile Trp Ala Phe Gly Val Leu Met Trp Glu Ile Tyr Ser
            580             585             590


Leu Gly Lys Met Pro Tyr Glu Arg Phe Thr Asn Ser Glu Thr Ala Glu
    595             600             605


His Ile Ala Gln Gly Leu Arg Leu Tyr Arg Pro His Leu Ala Ser Glu
    610             615             620


Arg Val Tyr Thr Ile Met Tyr Ser Cys Trp His Glu Lys Ala Asp Glu
625             630             635             640


Arg Pro Ser Phe Lys Ile Leu Leu Ser Asn Ile Leu Asp Val Met Asp
            645             650             655


Glu Glu Ser
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<210> 5
<211> 37
<212> DNA
<213> Artificial sequence

<220>
<223> Artificial = primer

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<210> 6
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<212> DNA
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<213> Artificial sequence .

<220>
<223> Artificial = primer

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<210> 7
<211> 37
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<220>
<223> Artificial = primer

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<210> 8
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<212> DNA
<213> Artificial sequence

<220>
<223> Artificial = primer

<400> 8
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<210> 9
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Artificial = primer

<400> 9
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<210> 10
<211> 33
<212> DNA
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<220>
<223> Artificial = primer

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<210>  12
<211>  38
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<400>  12
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